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SYNTHESIS AND USING OF 10-HYDROXY-3,3,6,6-TETRAMETHY- 9-(2-HYDROXYPHENYL)-1,2,3,4,5,6,7,8,9,10-DECAHYDROACRIDIN-1,8-DION AS ACID BASE TITRATION INDICATOR

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Abstract

10-hydroxydecahydryacridinedione derivative was synthesized by the reaction of dimedone, hydroxylamine and salicylaldehyde in dry pyridine. This substance is colorless in acidic and neutral and pink in base solutions. The acid dissociation constant of this compound in a hydroalcoholic solution was determined by the UV-visible spectroscopic technique. It was shown that the obtained compound can be used as an indicator for the titration of strong acids and bases. Titration standard 0.1 n solution of sodium hydroxide with standard 0.1 n solution of hydrochloric acid using of this compound as indicator has been successful

Keywords: 10-hydroxydecahydryacridinedione derivative, acid dissociation constant, indicator for the base-acid titration

1. Introduction

Decahydroacridinediones contain a 1,4-dihydropyridine ring as structural fragment and are available via various versions of Hantzsch synthesis [1–5]. These compounds exhibit a broad spectrum of biological activity [6, 7]. The dyes of the decahydroacridine series have been intensively studied due to the application of them, in particular, as laser dyes and fluorescent marks [8].

Earlier, we described the method synthesis of 10-hydroxy-1,2,3,4,5,6,7,8,9,10-decahydryacridine- 1,8-diones (1) by the reaction of cyclohexane-1,3-diones (3a,b), hydroxylamine (5) and aldehydes (4) in dry pyridine [3]. These substances are colorless in acidic and neutral and pink in base solutions. That is why they can be suitable acid-base titration indicators.

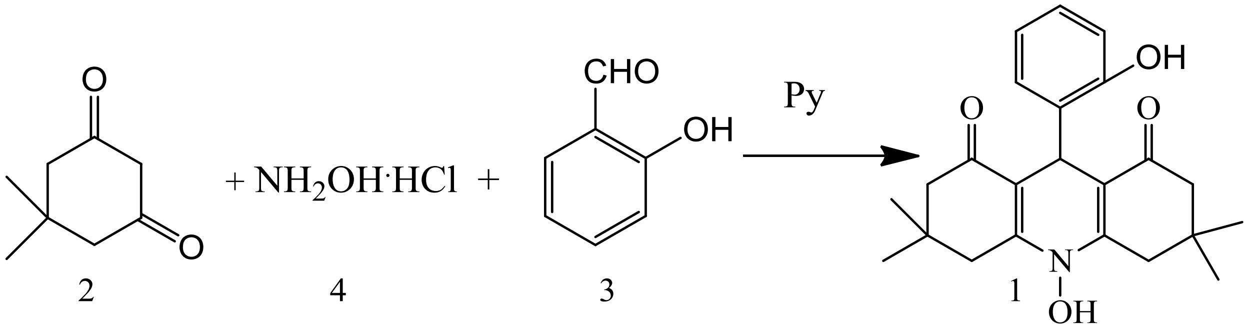
Here in we wish to report our results on synthesis of 10-hydroxy-3,3,6,6-tetramethyl-9-(2-hydroxyphenyl)-1,2,3,4,5,6,7,8,9,10-decahydroacridin-1,8-dion and the possibility of using this compound as indicator of acid-base titration (I).

2. Materials and Methods

The substance investigated was obtained by three-component heterocyclization of dimedone (2), hydroxylamine (4) with salicylaldehyde (3) in dry pyridineas as described in our article [3]. The reaction of cyclization proceeds as a result of heating of equimolar quantities of dimedone and hydroxylamine in a solution of dry pyridine with addition of aromatic aldehyde (Scheme 1).

Dimedone, hydroxylamine, salicylaldehyde and pyridine were acquired from Sigma-Aldrich.

Scheme 1.



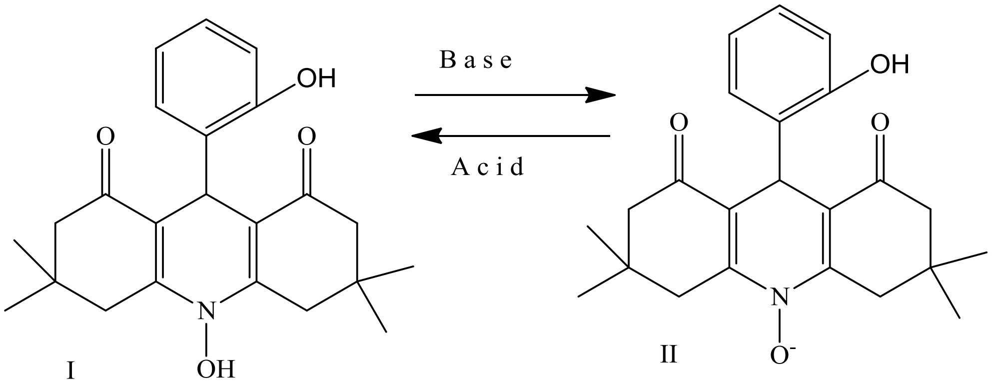
2.1. Procedure for synthesis of 10-hydroxy-3,3,6,6-tetramethyl-9-(2-hydroxyphenyl)-1,2,3,4,5,6,7,8,9,10-decahydroacridin-1,8-dion

The UV spectrum was recorded on a UV - 2501 PC spectrophotometer. The IR spectrum was obtained in KBr on a UR-20 spectrometer. The 1H and 13C NMR spectra of compound were examined on a Bruker AC-200 spectrometer at 200 and 50 MHz, respectively; tetramethylsilane was used as internal reference. The progress of reaction and the purity of product was monitored by TLC on Silufol UV-254 plates using EtOAc–hexane (1 : 1) as eluent; spots were visualized under UV radiation or by treatment with iodine vapor, followed by calcination at 250–350°C. The melting point was determined on a Boetius hot stage.
A mixture of 2.8 g (20 mmol) of 5,5-dimethylcyclohexane-1,3-dione (dimedone) and 0.76 g (11 mmol) of hydroxylamine hydrochloride in 15 ml of pyridine was heated for 1 h under reflux, 1.34 g (11 mmol) of salicylaldehyde was added, and the mixture was heated for 1 h more under reflux. It was then cooled to room temperature, diluted with 150 ml of water, and left to stand for 24 h. The precipitate was filtered off, washed with water (150 ml), and dried in air. Yield 3.47 g (91%), mp 203–205°C. IR spectrum, ν, cm^{-1}: 1150, 1240, 1380, 1495, 1600, 1630 – 1660 (C=C, C=O), 3260 (OH). UV spectrum, EtOH, nm (log ε): 255 (4.18); 395 (3.79), ^{1}H NMR spectrum (DMSO-d$_6$), δ, ppm: 0.97 s (6H, Me), 1.11 s (6H, Me), 2.05 and 2.22 (2H each, CH$_2$, AB system, J_{AB} = 17 Hz), 2.45 and 2.70 (2H each, CH$_2$, AB system, J_{AB} = 18 Hz), 5.08 s (1H, 9-H), 6.65 m (1H, H$_{arom}$), 6.90 m (2H, H$_{arom}$), 7.29 m (1H, H$_{arom}$). ^{13}C NMR spectrum (DMSO-d6), δC, ppm: 26.91 (Me), 29.46 (Me), 29.94(C9), 32.64 (C3, C6) 35.98 (C4, C5), 50.35 (C2, C7), 108.34 (C8a, C9a), 109.31 (C$_{arom}$), 111.83 (C$_{arom}$), 120.39 C$_{arom}$), 128.26 (C$_{arom}$), 137.07 (C$_{arom}$), 153.32 (COH), 154.03 (C4a, 10a), 196.91 (C1, C8). Found, %: C 72.30; H 7.05; N 3.77. C23H27NO4. Calculated, %: C 72.42; H 7.13; N 3.67.

This substance is colorless in acidic and neutral and pink in base solutions. That is why it can be suitable acid-base titration indicator. In the UV spectrum of hydroxydecahydryacridinedione (1) there is long-wave absorption band 395 nm, which maximum offset in the region of 504 nm when added to a solution of the base, which defines the possibility of the use of this compound as indicator basic media. It is obvious that the painted is the main form of (II), formed as a result of the tear-off of a proton from the acidic form (I) (Scheme 2).

By measuring the change in the optical density of absorption, proportional to the concentration of the painted form (II) depending on the pH-value of water or water-alcohol solutions of several hydroxydecahydryacridinediones (I), we calculated the values of acid dissociation constant (K_{Ind}) of these compounds, which allows you to set the color changing pH range of the indicator. It is determined by the value of the constants: $\Delta pH_{Ind} = pK_{Ind} \pm 1$.

Scheme 2.



The reversible dissociation process I ↔ II + H^+ is characterized by dissociation constant:

$$K_{diss.} = \frac{[H^+][II]}{[I]} \quad (1)$$

Where:

$[H^+]$, [I] and [II] are molar concentrations of proton, acid and its conjugate base (salt), respectively. To use this formula, it is necessary to determine the concentrations of all three components. Proton concentration was determined with a pH meter, a concentration of the base form - using spectrophotometric measurements. The mathematical expression for calculating the constants obtained as follows.

Denote the total concentration of both forms of C_0. The concentration of the main (colored) form denoted C, then the concentration of the acid form is C_0 - C expression for the dissociation constant is:

$$K_{diss.} = \frac{[H^+]\cdot C}{C_0 - C} \quad (2)$$

Bouguer - Lambert - Beer law [9] relates the molar concentration of the substance with the optical density of the maximum absorption of the solute (form):

$$D_{max.} = C_M \bullet L \bullet \varepsilon \text{ or } C_M = \frac{D_{max.}}{\varepsilon \cdot \lambda} \quad (3)$$

where $D_{max.}$ - The optical density of the absorption maximum, C_M - its molar concentration, *L* -cell width, cm, ε - molar extinction.

Using the expression of the optical density concentration, denoting
C_0 / L • ε = D_0 in the equation for the equilibrium constants have:

$$K_{diss.} = \frac{[H^+] \cdot D_{\max.}}{D_0 - D_{\max.}} \text{ or , } K_{diss.}(D_0 - D_{\max.}) = [H^+] \cdot D_{\max.}$$

If during the measurement the solution volume and the temperature does not change, then a number of successive measurements of pH values and corresponding densities longwave absorption maximum core mold (II) left side of the equation remains constant. Then, for two consecutive measurements (1 and 2) can be written:

$$K_{diss.} \cdot D_0 = K_{\text{дисс.}} \cdot D_1 + [H^+]_1 \cdot D_1 = K_{diss.} \cdot D_2 + [H^+]_2 \cdot D_2 \,,$$

then:

$$K_{diss.} = \frac{[H^+]_2 \cdot D_2 - [H^+]_1 \cdot D_1}{D_1 - D_2} \tag{5}$$

In the resulting expression is absent D_0, which means there is no need to prepare a certain concentration of solution of the substance (C_0) and using the resulting expression eliminates the need to weigh the samples and measuring the volume of the solution, and thus eliminates the associated measurement errors. Obviously, the accuracy of determining the dissociation constant depends on the range of measurement. At high pH, the concentration of the acid form is insignificant and low - basic. In the first case, the denominator in the expression for the dissociation constant tends to zero in the second - the numerator. Comparable amounts of both forms are solutions in which the pH is close to $_{\text{pKdiss.}}$ (at pH = pK concentrations of both forms of the same, that is, C = 0,5C_0).

2.2. Procedure for determining the dissociation constant

The total solution volume was 100 ml, wherein 50 ml buffer and 50 ml of ethanol. Buffer was Triss - 1.21 g per 100 ml. Needless active substance is 5 mg. A pH meter for measuring the pH of the solution was adjusted to 7 by adding hydrochloric acid. Then poured into a cuvette 2 ml of the solution and the absorption spectrum was recorded on a spectrophotometer UV - 2501 PC. Then, the pH was increased with concentrated KOH to pH 7.50, 8.00, 8.50, 9.00, respectively, and re-measured with a spectrophotometer. Registration density maximum absorption was carried out at 405 nm. The pH measurements were taken using an HI 221 pH meter.

3. Results and discussion

Results of measurements and calculations are given in the table 1. The resulting value $pK_{diss.}$ conversion process I ↔ II is 7.93 ±0.02.

Table 1.The results of optical density measurements of absorption maximum (D), pH and acid dissociation constant calculated 1,8-dioxodecahydroacridine (1) solution

No measuring	pH	$[H^+]$ mol/l	D	$^*K_{m,n}$	$^*pK_{m,n}$	$K_{average} \pm \Delta K$, $pK_{average} \pm \Delta pK$	$\Delta pH_{Ind} = pK_{Ind} \pm 1$
1	9,00	$1{,}00 \cdot 10^{-9}$	0,931	$K_{1,3}$ $1{,}20 \cdot 10^{-8}$	$pK_{1,3}$ 7,92	$K_{average} \pm \Delta K$	6,93 – 8,93
2	8,50	$3{,}16 \cdot 10^{-9}$	0,815	$K_{1,4}$ $1{,}20 \cdot 10^{-8}$	$pK_{1,4}$ 7,92	$(1{,}17 \pm 0{,}04) \cdot 10^{-8}$	
3	8,00	$10{,}00 \cdot 10^{-9}$	0,553	$K_{2,3}$ $1{,}13 \cdot 10^{-8}$	$pK_{2,3}$ 7,96	$pK_{average} \pm \Delta pK$	
4	7,50	$31{,}62 \cdot 10^{-9}$	0,277	$K_{2,4}$ $1{,}15 \cdot 10^{-8}$	$pK_{2,4}$ 8,06	7,93 ±0,02	
				$K_{3,4}$ $1{,}15 \cdot 10^{-8}$	$pK_{3,4}$ 7,94		

Note: $^*K_{m,n}$ and $^*pK_{m,n}$ are $K_{diss.}$ and $pK_{diss.}$ calculated using the formula (5) based on measurement of pH, D numbers m and n

The value of the dissociation constant indicates the possibility of using this compound as an indicator for the titration of strong acids and bases.

To confirm the possibility of using the compound as an indicator of acid-base titration, we performed titration standard 0.1 N solution of sodium hydroxide with standard 0.1 N solution of hydrochloric acid . The indicator used as a saturated solution this compound in ethyl alcohol, adding a few drops in the titrated solution. The volume of the titrated solution was 10.0 ml. It is obvious that in accordance with the law of equivalents for solutions of reactants if the concentrations of both solutions is the same with (0.1 N), and their volumes must be the same (10 ml) too.

As a control, the same titration performed with the same titrant solution using phenolphthalein as an indicator. The results are shown in Table 2. The volume of added titrant in ten experiments within the error of measurement of the volume of the solutions (±0.1 ml) correspond to the volumes defined solution, indicating that the obtained compound can be used as an indicator in the titration of strong acids and bases, such as the end point of our indicator is close to pH 7.

Table 2. The results of the titration of 10 ml of 0.1 N NaOH solution with 0.1 N hydrochloric acid solution using phenolphthalein and 10-hydroxy-3,3,6,6-tetramethyl-9-(2-hydroxyphenyl)-1,2,3,4,5,6,7,8,9,10-decahydroacridine-1,8-dion as indicator

indicator	No. of experience									
	1	2	3	4	5	6	7	8	9	10
	The volume of added titrant (0.1 N HCl), ml									
phenolphthalein	9,9±0,1	10,0±0,1	9,9±0,1	10,1±0,1	10,0±0,1	10,1±0,1	10,0±0,1	10,0±0,1	10,0±0,1	10,0±0,1
acridine	10,0±0,1	9,9±0,1	10,0±0,1	10,0±0,1	9,9±0,1	10,0±0,1	10,1±0,1	10,0±0,1	10,1±0,1	10,0±0,1

4. Conclusion

1. 10-hydroxy-3,3,6,6-tetramethyl-9-(2-hydroxyphenyl)-1,2,3,4,5,6,7,8,9,10-decahydroacridin-1,8-dion has been synthesized

2. The acid dissociation constant of the resulting compound in hydroalcoholic solution was determined

3. It was shown that this compound can be used as an indicator for the titration of strong acids and bases.

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